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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
1631	11

DATE MAILED: 01/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/723,256	DUNLAY ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30 and 44-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30 and 44-65* is/are rejected.

7)☒ Claim(s) *52* is/are objected to.

8)☒ Claim(s) *30 and 44-65* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Petition Decision

DETAILED ACTION

Applicant's amendments and remarks in Paper No. 8, filed 11/13/02, are acknowledged. Amended claim 30 and new claims 44-65 are acknowledged.

Applicant's arguments, filed 11/13/02, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The corrected or substitute drawings were received on 11/13/02. These drawings have been approved by the draftsman and the petition for photographic drawings has been approved.

Claims 30 and 44-65 are herein under examination.

Claim Objection

Claim 52 is objected to because of the following minor informality: "cell" on line 1 should be in the plural form. Appropriate correction is requested.

Provisional Obviousness-Type Double Patenting

The Examiner acknowledges Applicants' acknowledgement that claim 30 is provisionally rejected under the doctrine of obviousness-type double patenting as being unpatentable over claim 24 of copending Application No. 09/724,376 and that this rejection will be addressed if the claims become allowable.

The rejection is reiterated and expanded upon from the previous Office Action and maintained for reasons of record.

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harrassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 U.S.P.Q. 2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985); In re Van Ornum 686 F.2d 937, 214 U.S.P.Q. 761 (C.C.P.A. 1982); In re Vogel, 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970); and , In re Thorington, 418 F.2d 528, 163 U.S.P.Q. 644 (C.C.P.A. 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application is shown to be commonly owned with this application. See C.F.R. § 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

Claims 30, 44-48, 50, 52-56, and 61-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24-29 and 44-54 of co-pending Application No. 09/724,376. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claims define the invention which is a machine readable storage medium with a program to detect the

distribution of cellular macromolecules between different cellular compartments. The aforementioned claims in the pending applications all provide programs, methods, and screening with fluorescence-based molecular reagents and computer-based feature extraction, data analysis, and automation. Thus, such similarity among the inventions creates the presence of overlapping embodiments.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION

Claims 30 and 44-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The support for the amended claim 30 and new claims 44-65 as pointed to by the applicant (throughout the specification, for example, page 31, line 14 to page 34, line 28 and in particular from page 68, line 16 through page 72, line 12) does not support the "first fluorescent reporter molecule," "second fluorescent reporter molecule," "third fluorescent reporter molecule," and "fourth fluorescent reporter molecule," in claim 30 (page 2, lines 7-16, 18-22,

and 25-26 and page 3, lines 3-4, 7-8, and 13), claim 44 (lines 1-2), claim 45 (lines 3-4), claim 46 (lines 3-4), claim 47 (line 2), claim 48 (lines 3-4), claim 49 (lines 3-4), claim 50 (line 2), claim 51 (lines 3-4), claim 52 (lines 2 and 4-5), claim 53 (line 2), claim 54 (line 3), claim 55 (line 3), claim 56 (line 3), claim 57 (line 4), claim 58 (lines 3-4), claim 59 (line 2), claim 60 (line 3), claim 62 (lines 1-2), and claim 64 (lines 2 and 5). Written basis is provided for cell's fluorescent molecules within the local cytoplasmic region and the movement of fluorescent molecules (page 34, lines 17-19), but not for the broadly mentioned first, second and third fluorescent reporter molecules in the claims. Because the introduction of "first fluorescent reporter molecule," "second fluorescent reporter molecule," and "third fluorescent reporter molecule" lacks written basis for amended and new claims 30, 44-60, 62, and 64, as filed in Paper No. 8, filed on 11/13/02, it is considered NEW MATTER. Claims 61, 63, and 65 are also rejected due to their dependency from claims 30 and 64.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30 and 44-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 30, line 10, recites the phrase "optionally an at least fourth fluorescent reporter molecule" which is vague and indefinite. It is unclear how the fourth fluorescent reporter

molecule can be "optional" when it is considered "at least" as well. Clarification of this discrepancy is requested. Claims 44-65 are also rejected due to their direct or indirect dependence from claim 30.

102 and 103 Rejections

The Applicants traverse the 102(b) rejection as anticipated by Akong et al. (P/N 5,670,113) and the 103(a) rejection as unpatentable over Akong et al. in view of Lee et al. (P/N 5,627,908). Applicant states Akong et al. do not teach or suggest a machine readable storage medium comprising a program containing a set of instructions for causing a cell screening system to detect the distribution of one or more macromolecule of interest between two or more different cellular compartments on or in individual cells. Applicants state the prior art references do not teach all of the limitations in the claims. As claims have now been amended and added, these claims and accompanying traversals will be addressed below.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence

to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

The Applicants maintain that the Akong et al. in view of Lee et al. does not teach or suggest all of the claim limitations. Further explanation of the prior art rejections is described below.

Claims 30, 61, 64, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akong et al. (P/N 5,670,113) in view of *In re Venner*.

Akong et al. teach an automated measurement apparatus and computer-controlled methods to screen cells to which a fluorescent reagent has been added and identify sample attributes associated with these cells (abstract and col. 1, lines 11-18 and 40-43). Akong et al. teach plate readers which read (scan) an array of wells (col. 1, lines 40-43), including their invention that can measure at least one attribute (col. 2, lines 65-66) by emitted light (col. 3, lines 36-46). The biological samples that can be identified include proteins such as enzymes (col. 1, lines 18-20) and cell surface ion channels and receptors (col. 2, lines 10-14) which fall under the categories of first or second fluorescent reporter molecules in the instant invention. The mask as described in the instant specification is a binary image with the objects displayed in white and the background displayed in black (page 32, lines 19-21). Akong et al. teach the background fluorescent levels may occur in the sample before the reagent is added which warrants the measurement of background (pre-reagent) values (intensity) to be incorporated in the post-reagent analysis (col. 3, lines 47-56), effectively creating a mask. Akong et al. teach taking

multiple fluorescent measurements before, during and after the reagent is pumped into the wells (col. 4, lines 16-21) as a variety of agents may be added to the wells once or in multiple times (col. 4, lines 37-40). Akong et al. teach the method of testing the cellular response to the added reagents (col. 4, lines 64-67) and measuring the changes in fluorescent intensity to detect a change in the concentration of molecules (col. 5, lines 1-9). Akong et al. teach that this assay can include control samples (col. 5, line 37), as well as single or sequential additions of reagents (col. 5, lines 39-41). Akong et al. teach that this assay may include living cells (col. 5, line 18). Akong et al. teach this assay encompasses the detection differences in fluorescence intensities in a solution as a consequence of a cellular event which allows the assay to be used on any compound capable of differential fluorescence to change in response to a cellular event (col. 27, lines 15-34). Akong et al. teach the use of various fluorescent indicator (reporter) molecules, such as calcium-sensitive, chloride-sensitive, sodium-sensitive, and potassium-sensitive fluorescent indicators for these assays (col. 17, lines 25-40, col. 22, lines 18-41, and Table on cols. 21 and 22).

Although Akong et al. teach this method on a computer-driven apparatus, they do not teach having this program on a machine readable storage medium using computer-executable instructions. In re Venner 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) states that it is obvious to computerize a manual activity. The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over prior art as stated in MPEP § 2144.04, Part III. A skilled artisan in the art would have been motivated to enhance the procedures of detecting distribution of cellular macromolecules, as stated by Akong et al., by including these steps on a computer readable

medium in order to easily and efficiently gain an understanding of the roles of compounds in drug screening assays, as stated by Akong et al. (abstract). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to place computer-executable instructions on a machine readable storage medium for a manual activity (as discussed by *In re Venner*) such as the basic identification of macromolecular distribution in cells (as stated by Akong et al.), because this information would enhance and quicken access to the identification of compounds to be used as drugs, as stated by Akong et al. (abstract).

Thus, Akong et al., in view of *In re Venner*, motivate claims 30, 61, 64, and 65.

Claims 30, 44-45, 48, 51, 61, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akong et al. (P/N 5,670,113), in view of Lee et al. (P/N 5,627,908) and *In re Venner*.

Akong et al. and *In re Venner* teach a machine readable storage medium and an automated measurement apparatus and computer-controlled methods to screen cells to detect macromolecular distribution in cells (see 103(a) rejection above). However, Akong et al. does not teach reference of both a cytoplasmic mask and a nuclear mask.

Lee et al. disclose the use of a computer to identify multiple cell patterns (col. 5, lines 24-25) via an image analysis system (col. 14, lines 54-55) on fixed cells on a slide (col. 5, lines 34-39). While providing over 15,000 fields of view for one specimen, not all fields are of interest (col. 14, lines 58-60). A mask is provided to express a unique identification value including size, shape and location for the object of interest (col. 15, lines 15-18) for both the nucleus and cytoplasm of each cell (col. 15, lines 29-30). Lee et al. teach that the brightness of the object

within the predetermined range (nucleus, cytoplasm, or background) is determined (col. 15, lines 42-46 and col. 16, lines 3-4). Lee et al. disclose the background can be normalized to aid in detecting images where the objects of interest include two portions having different levels of brightness (intensity) such as the nucleus and cytoplasm (col. 17, lines 53-66). Lee et al. disclose the act of eroding the objects of a mask (such as the nuclear mask) and then dilating them by a second predetermined amount where the amount of erosion exceeds the amount of dilation to separate connected objects and create another mask (cytoplasmic mask, in this case) (col. 20, lines 34-54).

Akong et al. states the need for rapidly screening compounds to determine the effects and concentrations of molecules within a cell during drug screening in order to identify potential pharmaceuticals (col. 2, lines 10-14 and col. 5, lines 10-19). Akong et al. use computer-controlled methods to assay the activity and distribution of molecules within cells, particularly the cytoplasm of a cell (col. 2, lines 56-67; col. 3, lines 1-2; and col. 5, lines 4-9). A skilled artisan would have been motivated to enhance the machine readable storage medium with a method of identifying the distribution of molecules via fluorescent indicator molecules, as stated by *In re Venner* and Akong et al., by including further steps of dividing the cell area under examination in order to normalize variations and gain an accurate and rapid view of a particular area of interest, as stated by Lee et al. (col. 1, lines 7-8 and col. 15, lines 10-13). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to further compartmentalize the areas undergoing optical cell screening analyses on a machine readable storage medium (as stated by Akong et al. and *In re Venner*) via the use of nuclear and cytoplasmic masks (as stated by Lee et al.), because this would enhance the

understanding and create a quicker and more accurate view of compounds that affect cells under study, as stated by Akong et al. (abstract).

Thus, Akong et al., in view of Lee et al. and *In re Venner*, motivate claims 30, 44-45, 48, 51, 61, and 63-65.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

January 21, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER